

Application No.: 10/616,082  
Amendment Date: 20 Mar 2009  
Reply to Office Action of: 23 Jan 2009

AMENDMENTS TO THE DRAWINGS:

The attached sheets of drawings includes changes to Figure 1A. The replacement sheet for Figure 1A replaces the original sheet for Figure 1A. In Figure 1A, an incorrectly drawn element has been corrected in the replacement sheet for Figure 1B. A replacement sheet for Figure 1B is included for consistency and to provide a better file copy of Figure 1B.

Attachment:

Replacement Sheets for Figures 1A and 1B  
Annotated Sheets Showing Changes to Figure 1A

REMARKS/ARGUMENTS

Claims 1-2, 6, 10-16, 18, 19, 26-30, and 57-67 are pending. Claims 3, 4, 5, 7, 8, 9, 17, 20-25, and 31-56 are cancelled. Claims 59-67 are new.

Claims 1, 2, 10, 12, 14-16, 18-19, 57-58 were amended in an effort to address specific issues raised by the Examiner. These amendments are not believed to introduce new matter into the application.

New claims 59-67 limit the host cell to “yeast” but otherwise are similar to claims 1, 10-13, 27-30, respectively. Support for “expressing a nucleic acid encoding the recombinant glycoprotein in a yeast host cell that is diminished or depleted in the activity of an initiating  $\alpha$ -1,6-mannosyltransferase and expresses an  $\alpha$ -1,2-mannosidase activity, a GlcNAc transferase I (GnT I) activity, and a chimeric mannosidase activity” can be found throughout the specification. Specific examples can be found in the Examples which illustrate the method using the yeast host cell *Pichia pastoris* host cells that are diminished or depleted in the activity of an initiating  $\alpha$ -1,6-mannosyltransferase (*ZOCH1*) and express an  $\alpha$ -1,2-mannosidase activity, a GlcNAc transferase I (GnT I) activity, and a chimeric mannosidase activity (See Examples 3, 4, 5, and 8). These new claims are not believed to add new matter.

Replacement sheets replacing Figures 1A and 1B are provided. Figure 1A as shown on the annotated copy incorrectly showed the linkage of the outer mannose residues on the hypermannosylated *N*-glycan in the last step. This is believed to be an obvious error that would be readily apparent to a person skilled in the art. No substantive changes were made to Figure 1B; however, a replacement Figure 1B is included to keep the styles between Figures 1A and 1B consistent and to provide better copies of the drawings for the file. The replacement drawings are not believed to introduce new matter into the application.

I. Claims 14-19 objections

Claims 14-19 were objected to because the claims refer to “mannosidase enzyme” when for consistency the claims should recite “chimeric mannosidase enzyme” to maintain consistency. The claims have been amended as suggested by the Examiner.

In light of the amendments to the claims, the basis for the objections should have been removed. Reconsideration of the objection is requested.

II. Claims 1, 2, 6, 10-16, 19, 26-30, 57, and 58 rejected under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 5-16, 18-30, 57, and 58 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. In particular, the rejection states "In claims 1 and 2, initially it is claimed that an N-glycan comprising GlcNAcMan<sub>5</sub>GlcNAc<sub>2</sub> is produced. Then later in the claim, an oligosaccharide substrate is used to produce a desired N-glycan, with the desired N-glycan having the oligosaccharide branch Man α1,3 (Man α1,6) Manβ1,4-GlcNAβ1,4-GlcNAc-Asn. It is unclear whether the oligosaccharide branch Man α1,3 (Man α1,6) Manβ1,4-GlcNAβ1,4-GlcNAc-Asn is added to GlcNAcMan<sub>5</sub>GlcNAc<sub>2</sub>, or whether it is added to a different substrate. If Man α1,3 (Man α1,6) Manβ1,4-GlcNAβ1,4-GlcNAc-Asn is not added to GlcNAcMan<sub>5</sub>GlcNAc<sub>2</sub>, then it is unclear what purpose GlcNAcMan<sub>5</sub>GlcNAc<sub>2</sub> has in the method."

Independent claims 1 and 2 have been amended to more clearly define the applicant's invention and claim 59 has been introduced to clearly define the applicant's invention. The applicant's invention is a method for making a recombinant glycoprotein in a uni- or multicellular fungal (or yeast) host cell by expressing a chimeric mannosidase II enzyme in a host cell that expresses an α-1,2-mannosidase and a GlcNAc transferase I (GnT I) and is diminished or depleted in the activity of an initiating α-1,6-mannosyltransferase, wherein expression of said chimeric mannosidase in the host cell produces one or more N-glycan structures on a recombinant glycoprotein expressed in said host cell, wherein the N-glycan is produced within the host cell at a yield of at least 10 mole percent and wherein the N-glycan is characterized as having at least the oligosaccharide branch Manα1,3 (Manα1,6) Manβ1,4-GlcNAc β1,4-GlcNAc-Asn.

It is believed the currently amended claims and new claim 59 clearly set forth what the applicant's invention is. In light of the amendments to the claims, reconsideration of the rejection is requested.

III. Claims 1, 2, 6, 10-16, 19, 26-30, 57, and 58 rejected under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 6, 10-16, 19, 26-30, 57, and 58 rejected under 35 U.S.C. § 112, second paragraph, on the premise that the term "desirable N-glycan" in claims 1 and 2 is a relative term which renders the claims indefinite. Claims 1 and 2 and claims 57-58 have been amended to cancel the term. Claim 1 has also been amended to provide an antecedent basis for

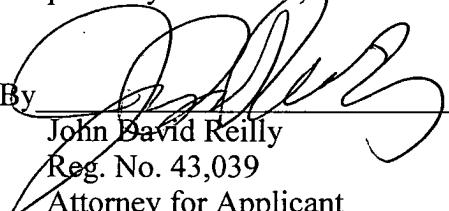
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the term "oligosaccharide substrate" in claim 6. In light of the amendments, it is believed that the claims satisfy the requirements of 35 U.S.C. § 112, second paragraph. Reconsideration of the rejection is requested.

In view of the foregoing remarks and amendments, it is believed that the grounds of rejections have been overcome and that the claims are in proper condition for allowance. Accordingly, Applicants respectfully request that all of the rejections be withdrawn and a Notice of Allowance be forwarded to the Applicants. The Examiner is invited to contact Applicants' Attorney at the telephone number given below, if such would expedite the allowance of this application.

CONDITIONAL PETITION

Applicant hereby makes a Conditional Petition for any relief available to correct any defect in connection with this filing, or any defect remaining in this application after this filing. The Commissioner is authorized to charge deposit account 13-2755 for the petition fee and any other fee(s) required to effect this Conditional Petition.

Respectfully submitted,  
  
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Date: March 20, 2009

# Annotated Sheet

Express Mail Label  
No. EV270268390US



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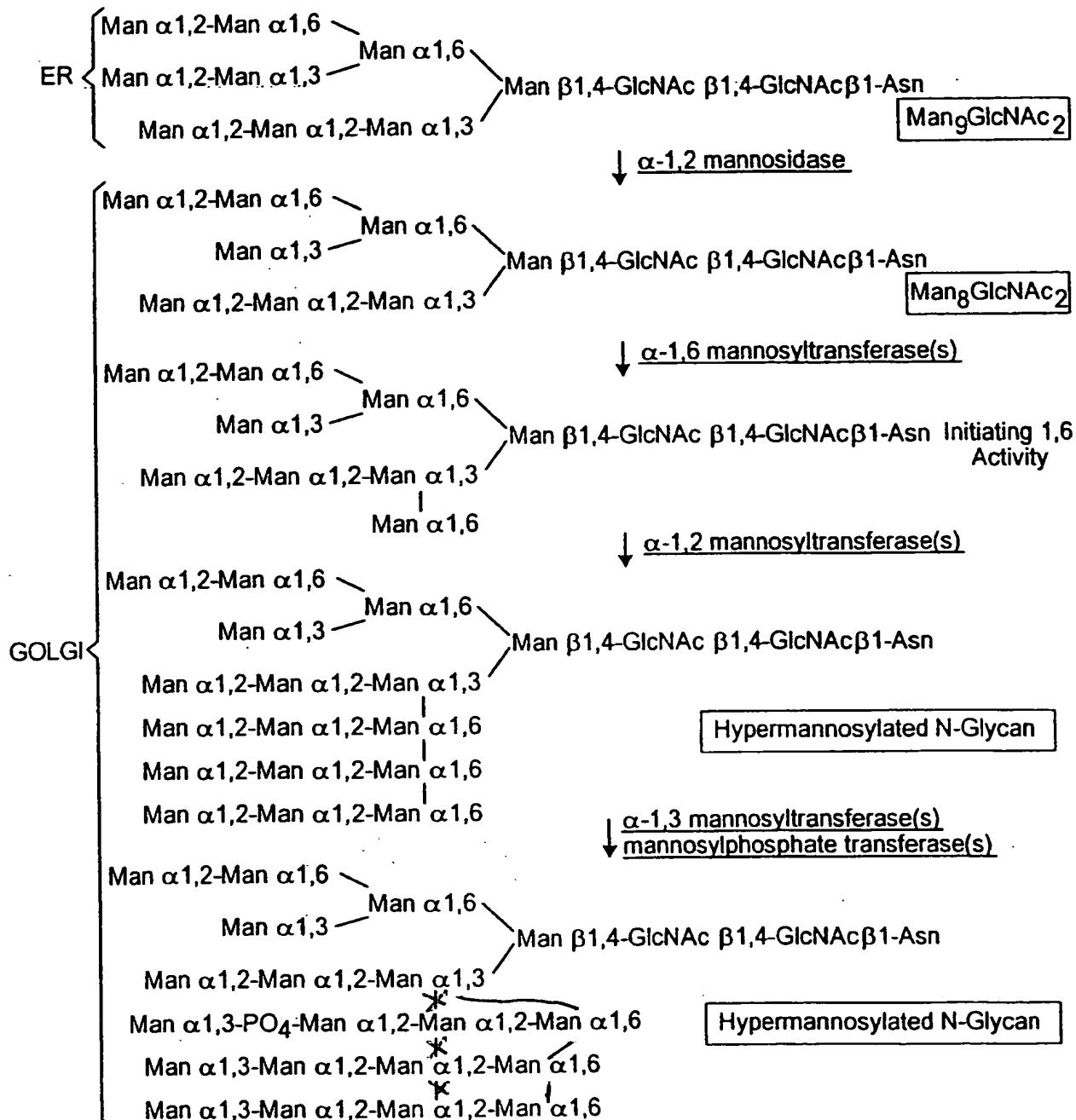


FIG. 1A

# Annotated Sheet

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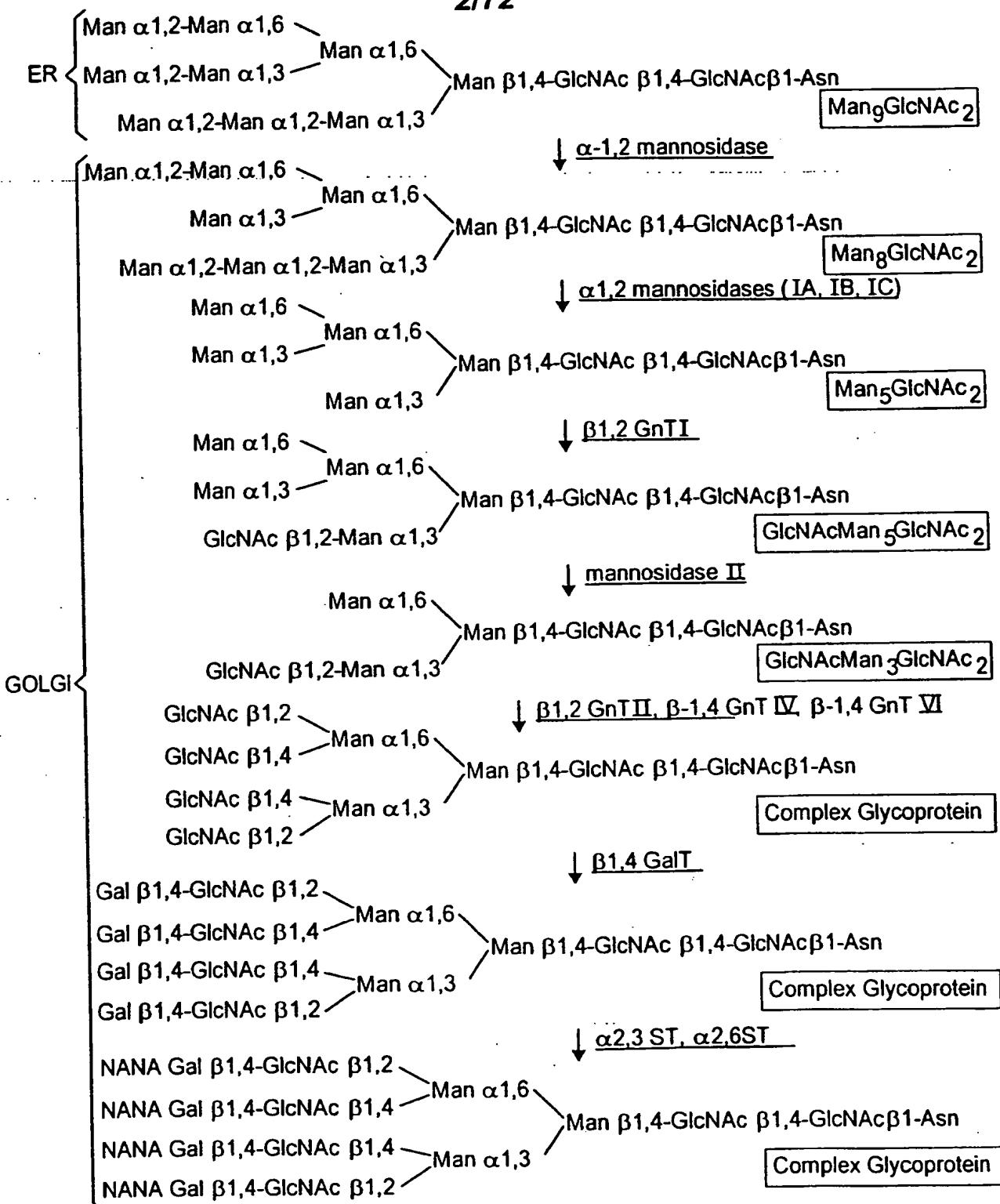


FIG. 1B